UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,835	07/14/2003	Thomas F. Meyer	0147-0250P	8238

2292 7590 05/05/2006

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/617,835	MEYER ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 02/13/06 has been acknowledged.
Claims 1-9 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 101

Claims 1-9 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well-established utility, for the same reasons of record as set forth in the office action mailed on 09/13/05.

The instant claims are drawn to an isolated nucleic acid sequence and/or any variant thereof that encodes a lipoprotein or any fragment thereof that mediates adhesion of Neisseria cells to human cells. The specification asserts that SEQ ID NO:4 encodes a polypeptide designated as OrfB, which does not have homology to any presently known proteins. The specification asserts that this protein possesses the ability to form a complex with the protein PilC and to induce either alone or in combination with OrfA the adhesion to human cells (Spec. para. 0066 or page 15).

The instant invention is not considered to have a specific and/or substantial utility, since the instant specification fails to establish that that the

disclosed polynucleotide sequences (SEQ ID NO:4) encodes an amino acid which that mediates adhesion of Neisseria cells to human cells explicitly or implicitly as putatively asserted by the instant specification.

The state of the art at the time of filing teaches that interaction of *Neisseria with human cell is complex and is dependent upon the PilC protein expression.* Pathogenic *Neisseria* express type IV pili (tfp), which have been shown to play a central role in the interactions of bacteria with their environment. The regulation of piliation constitutes a central element in bacterial life cycle. The PilC proteins are outer membrane-associated proteins that have a key role in tfp biogenesis. In pathogenic *Neisseria*, tfp are responsible for adhesion to human host cells. Pilus retraction is responsible for twitching motility, and has been shown to play a central role in the interactions of pathogenic *Neisseria* with human cells. Furthermore Pilus retraction is associated with the relocalisation of mature pilin subunits along the cytoplasmic membrane. Among the components of the neisserial tfp machinery, the PilC proteins play a crucial but still enigmatic role. They are associated with the outer membrane but can also be recovered from purified pili. PilC-null strains show impairment in pilus expression and are not competent for transformation. However, the mechanism by which the PilC proteins promote piliation remains unknown. It is presumed they act as pilus tip adhesins in *Neisseria gonorrhoeae* and the two *pilC loci* harboured by this species are functionally interchangeable. On the other hand, in *Neisseria meningitidis*, only PilC1 is equivalent to the gonococcal PilC proteins and promotes adhesion. PilC2, which is independently expressed from PilC1, fails to promote adhesion despite identical functions in piliation and transformation competence (see Morand et al The EMBO Journal 23(9): 2009–2017, 2004). Since the specification fails to provide any evidence, which establishes that the amino acid sequences of SEQ ID NO:4 encodes for a polypeptide that mediates adhesion of Neisseria cells to human cells explicitly or implicitly, the invention as claimed herein is not supported by either a specific asserted utility or a well-established utility.

In addition, the scope of invention as claimed encompasses any and all variants of nucleotide sequences encoding polypeptide that mediates adhesion of Neisseria cells to human cells (i.e. any fragment or variant encoded any hybridization product and/or having 5% variation). The variations as claimed encompasses the conserved motifs that may be germane to the adhesion of Neisseria cells to human cells (as claimed). It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function could be ascribed to the gene product (as asserted).

The instant specification does not comply with 35 U.S.C. 101 and 112 since nebulous expressions "biological activity" and "biological properties" do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and not after someone else identify a utility that had not been disclosed in the specification. The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner. For example, it cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and

Petrow, 153 USPQ 48 (CCPA 1967)). In instant case the mere association with Orf-A or PilC does not teach one skill in the art how to use the invention as claimed, since the disclosure is insufficient and requires further experimentation necessary to determine actual uses or possible lack of uses of the polypeptide, as well as how to employ them in a useful manner. Furthermore considering the instant specification, it cannot be presumed that the asserted use of SEQ ID NO:4 is useful under 35 USC 101/112 or that one skilled in the art will know "how to use" it, simply because polypeptide is associated with peptides that participates in PilC function. In view of the foregoing, one skilled in the art would not readily attribute the asserted biological activity to the nucleotide sequences that encodes SEQ ID NO:4

Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene product. The only immediate apparent utility for the instant invention would be further scientific characterization of the claimed nucleotide sequences as a putative adhesion protein that promotes the adhesion of Neisseria cells to any and all types human cells.

Claims 1-9 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth *above*, one skilled in the art clearly would not know how to use the claimed invention, or the same reasons of record as set forth in the office action mailed on 09/13/05.

Response to arguments (Utility/Enablement)

The applicant arguments regarding prior issue on pages 2-6 of response filed on 02/13/06 has been fully considered. The applicant argues that the specificaiton as filed on page 22, example-4 and table-1 demonstrates that OrfA-dependent modulation of PilC mediated adhesion function. The applicant argues that E. coli strain H2560 adhered to human epithelial cells. The applicant argues that H2560 is an E.coli HB101

with plasmid pES25, wherein the pES25 contains genomic fragement of N. gonorrhoeae of approximatly 11kb carrying the coding region orfA, orfB and orfl. The applicant admints that claim 1 is clearly directed to nucleic acids having a nucleotide sequence encoding the peptide sequence of SEQ ID NO:4 and related nucleic acids. However, the applicant argues that Examiner's attention is directed to the parent case, which has issued as U.S. Patent No. 6,617,128 with special reference to claim 6 which is limited to nucleotide sequences of SEQ ID NO:7. The applicant argues that present claims are not directed to methods of use but rather nucleic acids. The applicant argues that sspecification states that "fragments are understood to be parts of the nucleic acid molecules that are long enough to encode the protein described" (Specification, page 7). The applicant argues that the specification recites the following, "This protein possesses a biological activity that mediates the adhesion of Neisseria cells to human cells." (spec page 9).

However, applicant's arguments are found not persuasive. The instant invention is not considered to have a specific and/or substantial utility, since the specification as filed fails to establish that that the polynucleotide sequences of SEQ ID NO:4 encodes an amino acid which that mediates adhesion of Neisseria cells to human cells explicitly or implicitly as putatively asserted by the instant specification. The tablle-1 fails to show that genetically modified host cells encoding the polypeptide OrfB (encoded by SEQ ID NO:4) possess the ability to form a complex with the protein PilC and to induce either alone or in combination with OrfA the adhesion to human cells as asserted by the applicant. Furthermore SEQ ID NO:7 (OrfA) as claimed in the U.S. Patent No. 6,617,128 is structurally distinct polynucleotide encoding a functionally distinct protein. Therefore one would not reach to a conclusion that OrfB would have OrfA like activity.

The earlier office action provides clear evidence that the interaction of *Neisseria with human cell is complex and is dependent upon the PilC protein expression.* (see Morand et al The EMBO Journal 23(9): 2009–2017, 2004). Since the specification fails to provide any evidence, which establishes that the nucleic acid sequences of SEQ ID NO:4 encodes a polypeptide that mediates adhesion of Neisseria cells to human cells explicitly or implicitly, the invention as claimed herein is not supported by either a

specific asserted utility or a well-established utility. Since the invention as claimed is not supported by either a specific asserted utility or a well-established utility, it is not clear how one skilled in the art would use the nucleic acid sequences that encodes SEQ ID NO:4, especially in context to a polypeptide that mediates adhesion of Neisseria cells to human cells.

Claim Rejections - 35 USC § 112

Applicant's arguments, regarding Written description and related enablement issues, filed on 02/13/06, have been fully considered and are persuasive. The rejection of claims 1-9 has been withdrawn.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If

attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

SUMESH KAUSHAL
PRIMARY EXAMINER